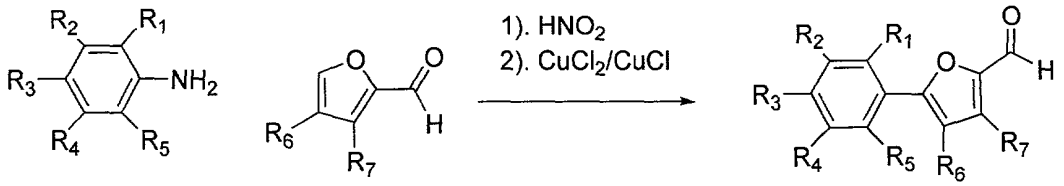
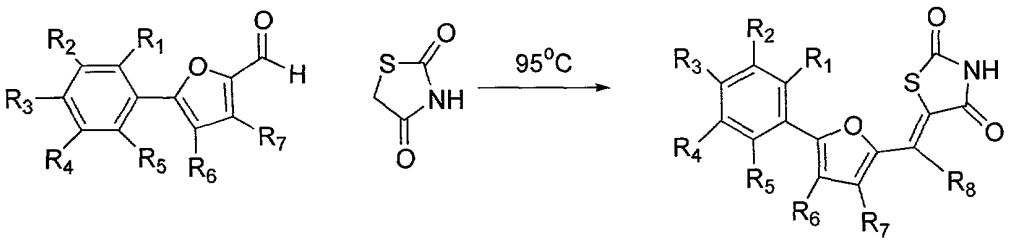


1

2

2-furaldehyde

3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe



3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe

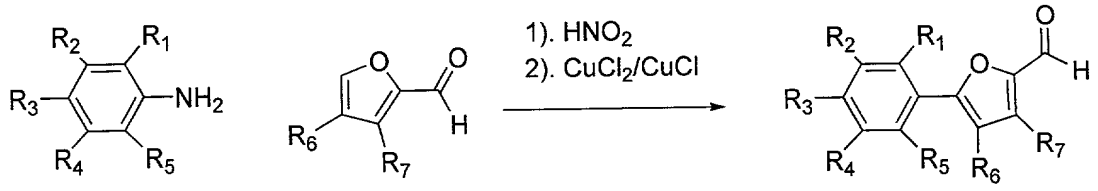
4

2,4-thiazolidinedione

5a R_3 = COOH
5b R_2 = COOH
5c R_3 = OH
5d R_3 = OH, R_2 = COOMe
5e R_3 = OH, R_2 = COOH
5f R_2 = NHAc
5g R_2 = OMe, R_3 = OMe

LiOH

FIGURE 1

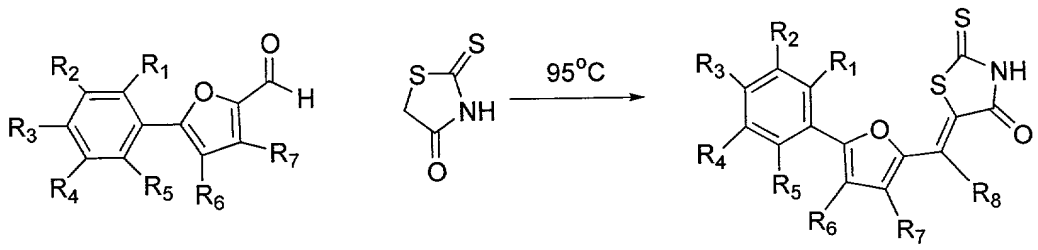


1

2

2-furaldehyde

3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe



3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe

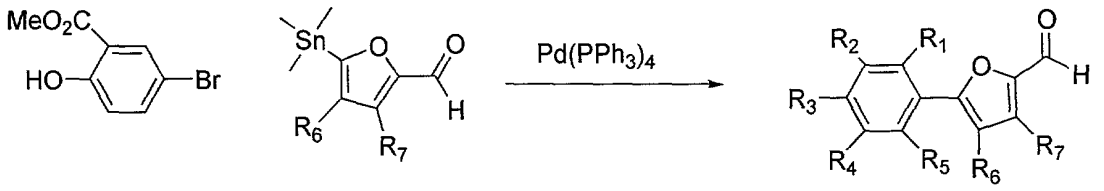
6

rhodanine

7a R_3 = COOH
7b R_2 = COOH
7c R_3 = OH
7d R_3 = OH, R_2 = COOMe
7e R_3 = OH, R_2 = COOH
7f R_2 = NHAc
7g R_2 = OMe, R_3 = OMe

LiOH

FIGURE 2

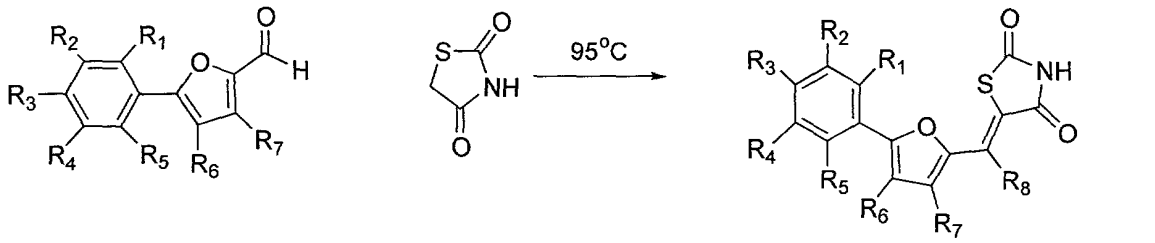


8

9

5-trimethylstannanyl-furan-2-carbaldehyde

3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe



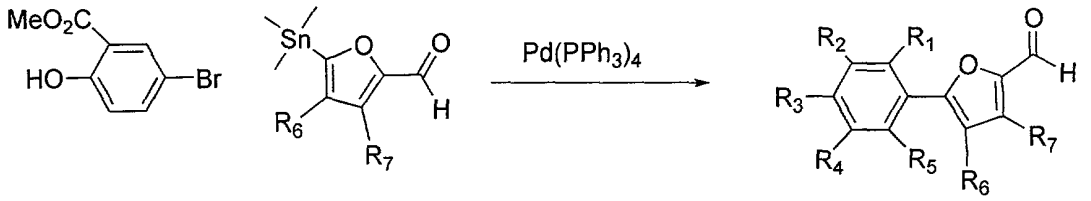
3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe

4
2,4-thiazolidinedione

5a R_3 = COOH
5b R_2 = COOH
5c R_3 = OH
5d R_3 = OH, R_2 = COOMe
5e R_3 = OH, R_2 = COOH
5f R_2 = NHAc
5g R_2 = OMe, R_3 = OMe

LiOH

FIGURE 3

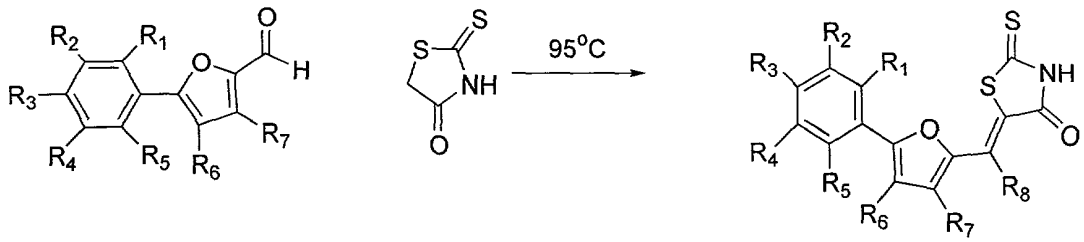


8

9

5-trimethylstannanyl-furan-2-carbaldehyde

3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe



3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe

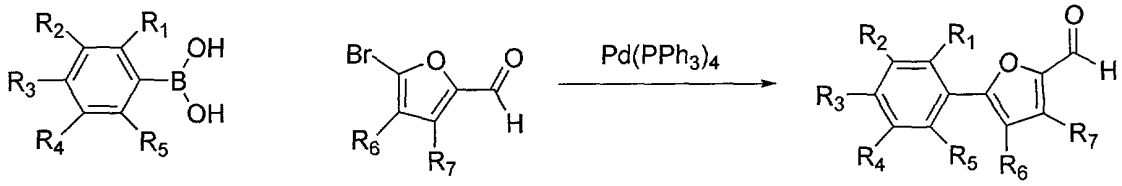
6

rhodanine

7a R_3 = COOH
7b R_2 = COOH
7c R_3 = OH
7d R_3 = OH, R_2 = COOMe
7e R_3 = OH, R_2 = COOH
7f R_2 = NHAc
7g R_2 = OMe, R_3 = OMe

LiOH

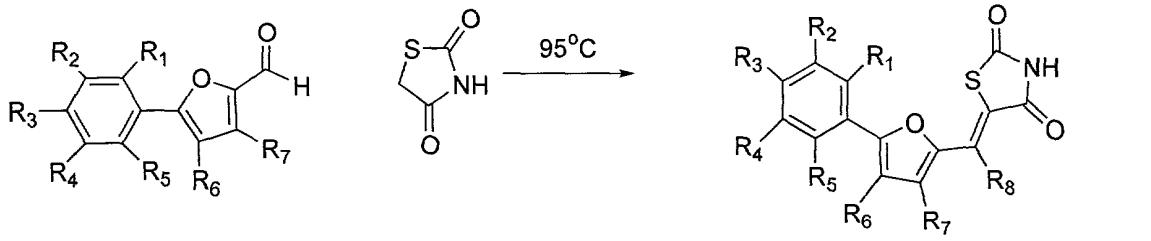
FIGURE 4



10a R_2 = NHAc
10b R_2 = OMe, R_3 = OMe

11
5-bromo-2-furaldehyde

3a R = 4-COOH
3b R = 3-COOH
3c R = 4-OH
3d R = 4-OH, 3-COOMe
3f R = 3-NHAc
3g R= 3-OMe, 4-OMe

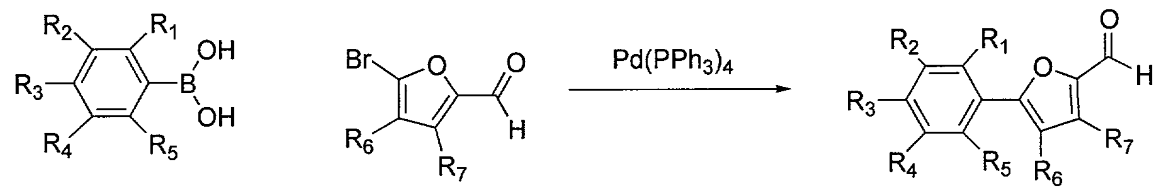


3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe

4
2,4-thiazolidinedione

5a R_3 = COOH
5b R_2 = COOH
5c R_3 = OH
5d R_3 = OH, R_2 = COOMe
5e R_3 = OH, R_2 = COOH
LiOH
5f R_2 = NHAc
5g R_2 = OMe, R_3 = OMe

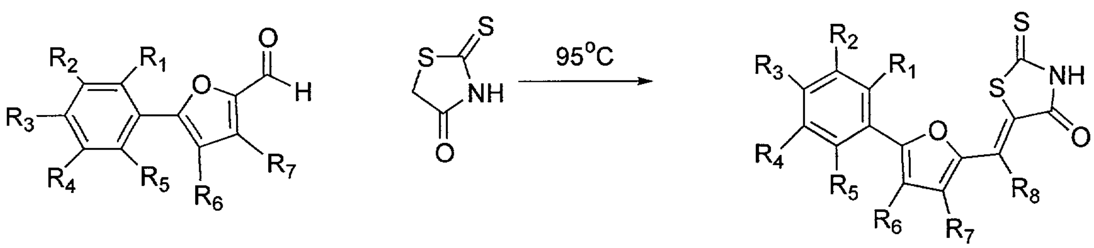
FIGURE 5



10a R_2 = NHAc
10b R_2 = OMe, R_3 = OMe

11
5-bromo-2-furaldehyde

3a R = 4-COOH
3b R = 3-COOH
3c R = 4-OH
3d R = 4-OH, 3-COOMe
3f R = 3-NHAc
3g R= 3-OMe, 4-OMe



3a R_3 = COOH
3b R_2 = COOH
3c R_3 = OH
3d R_3 = OH, R_2 = COOMe
3f R_2 = NHAc
3g R_2= OMe, R_3 = OMe

6
rhodanine

7a R_3 = COOH
7b R_2 = COOH
7c R_3 = OH
7d R_3 = OH, R_2 = COOMe
7e R_3 = OH, R_2 = COOH
(7d → 7e: LiOH)
7f R_2 = NHAc
7g R_2 = OMe, R_3 = OMe

FIGURE 6

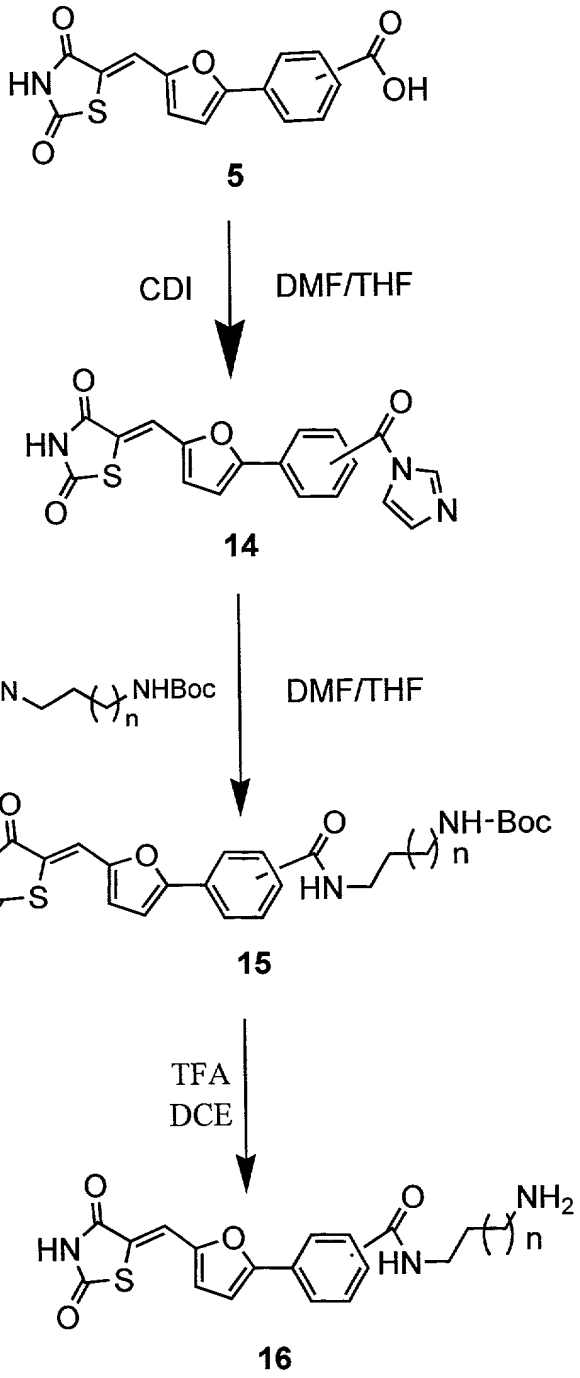


FIGURE 7

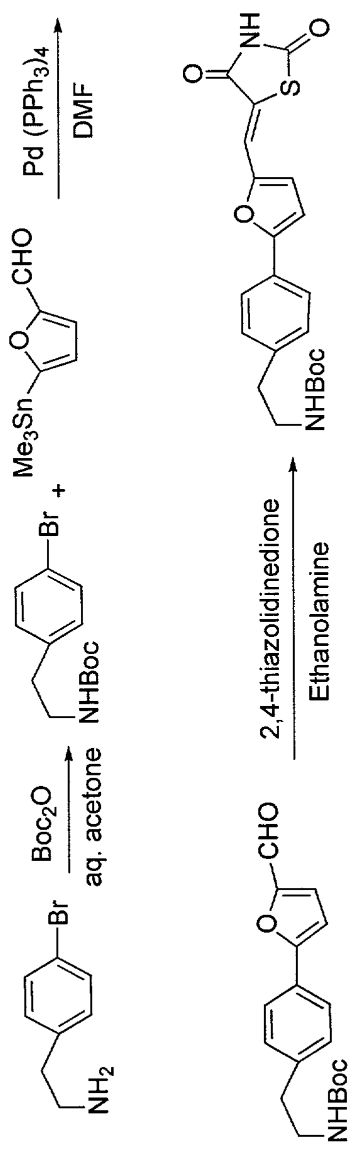
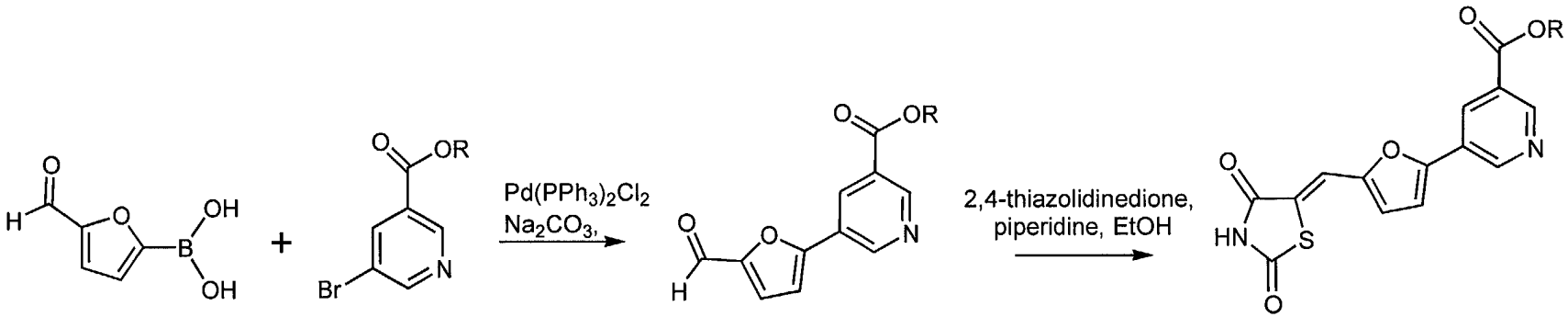


FIGURE 8



17

18a: R = H
18b: R = $NH(CH_2)_3OH$

19a: R = H
19b: R = $NH(CH_2)_3OH$

20a: R = H
20b: R = $NH(CH_2)_3OH$

FIGURE 9

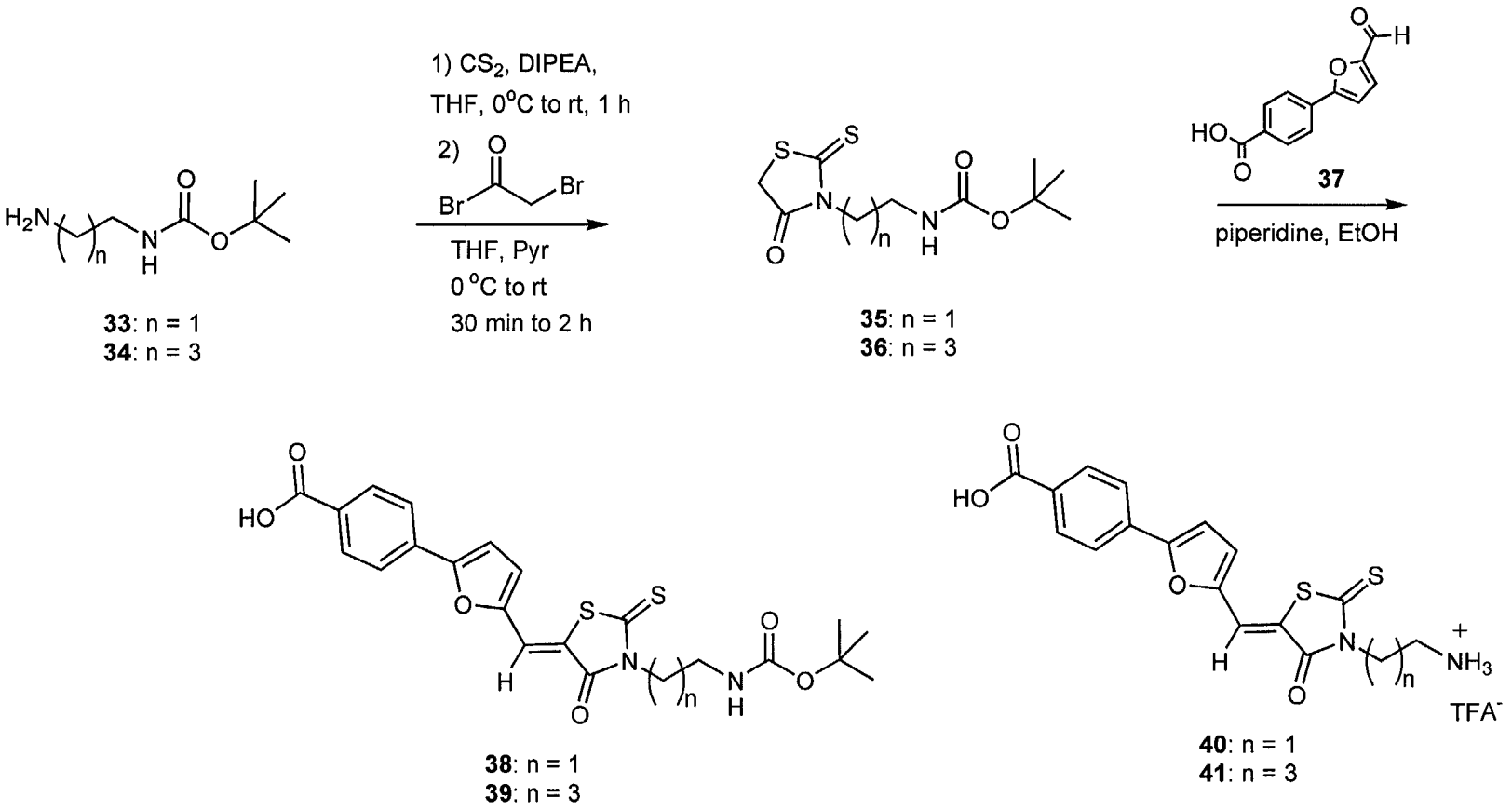

1) CS_2, DIPEA,
THF, 0°C to rt, 1 h
2)
THF, Pyr
0 °C to rt
30 min to 2 h
piperidine, EtOH
37
33: n = 1
34: n = 3
35: n = 1
36: n = 3
38: n = 1
39: n = 3
40: n = 1
41: n = 3
TFA⁻

FIGURE 10

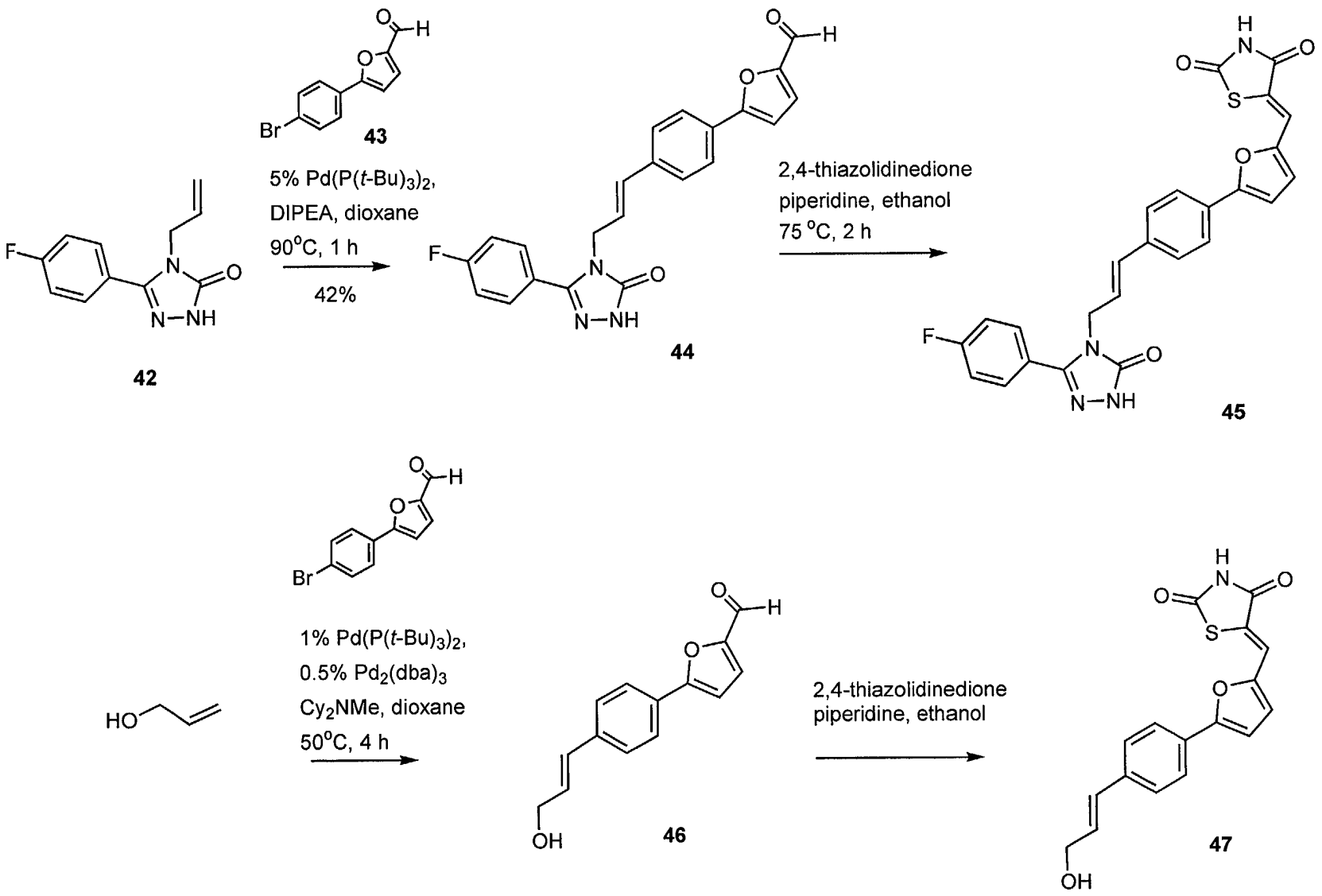


FIGURE 11

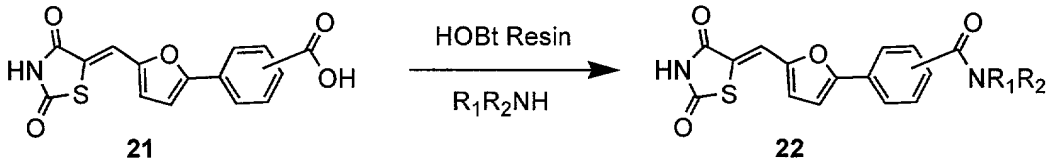


FIGURE 12a

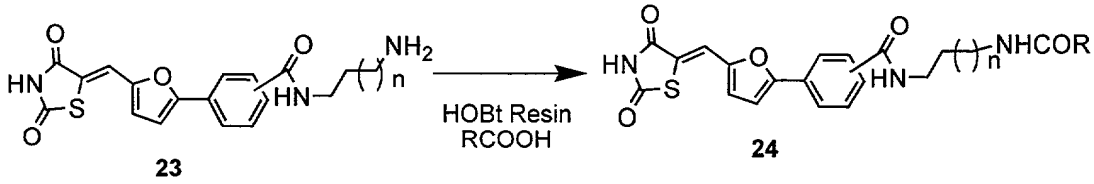


FIGURE 12b

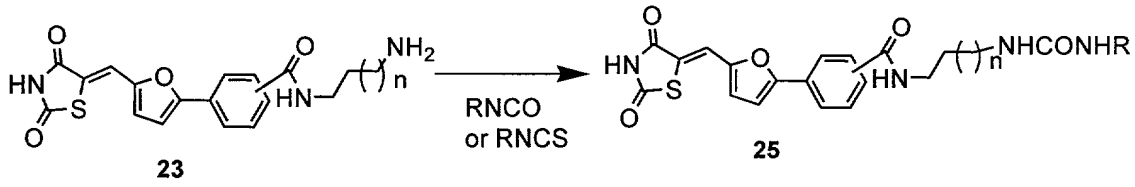


FIGURE 12c

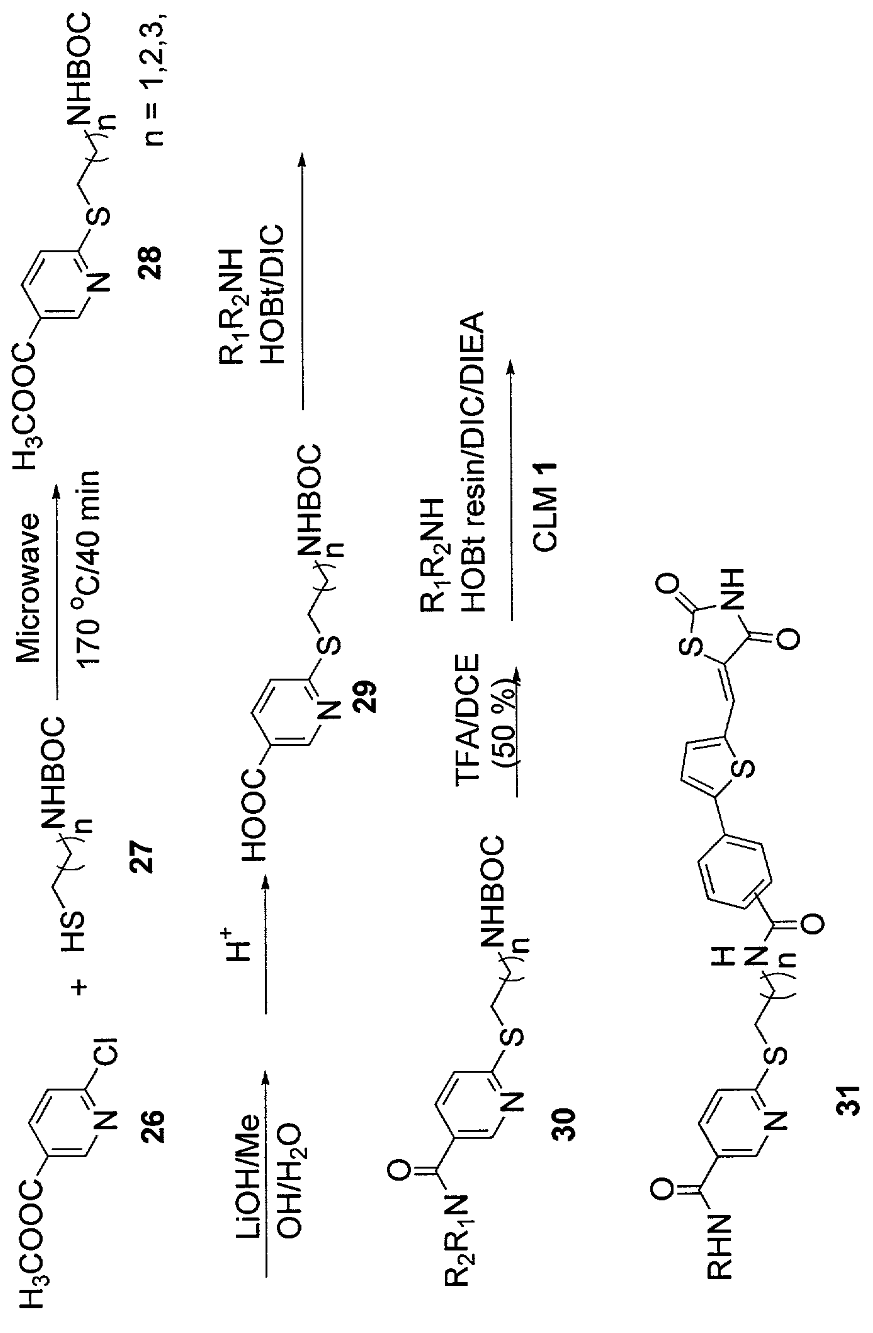

H3COOC
Cl
26
HS
NHBOC
27
Microwave
170 °C/40 min
28
n = 1,2,3,
LiOH/Me
OH/H2O
H+
HOOC
29
R1R2NH
HOBt/DIC
R2R1N
30
TFA/DCE
(50 %)
R1R2NH
HOBt resin/DIC/DIEA
CLM 1
RHN
31

FIGURE 13

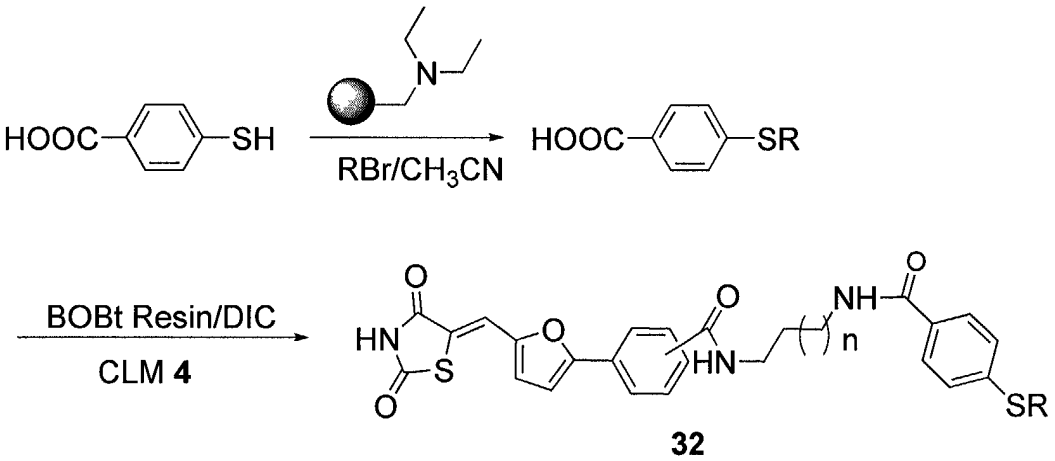

HOOC
SH
N
RBr/CH3CN
HOOC
SR
BOBt Resin/DIC
CLM 4
O
HN
S
O
O
O
HN
NH
n
O
SR
32

FIGURE 14

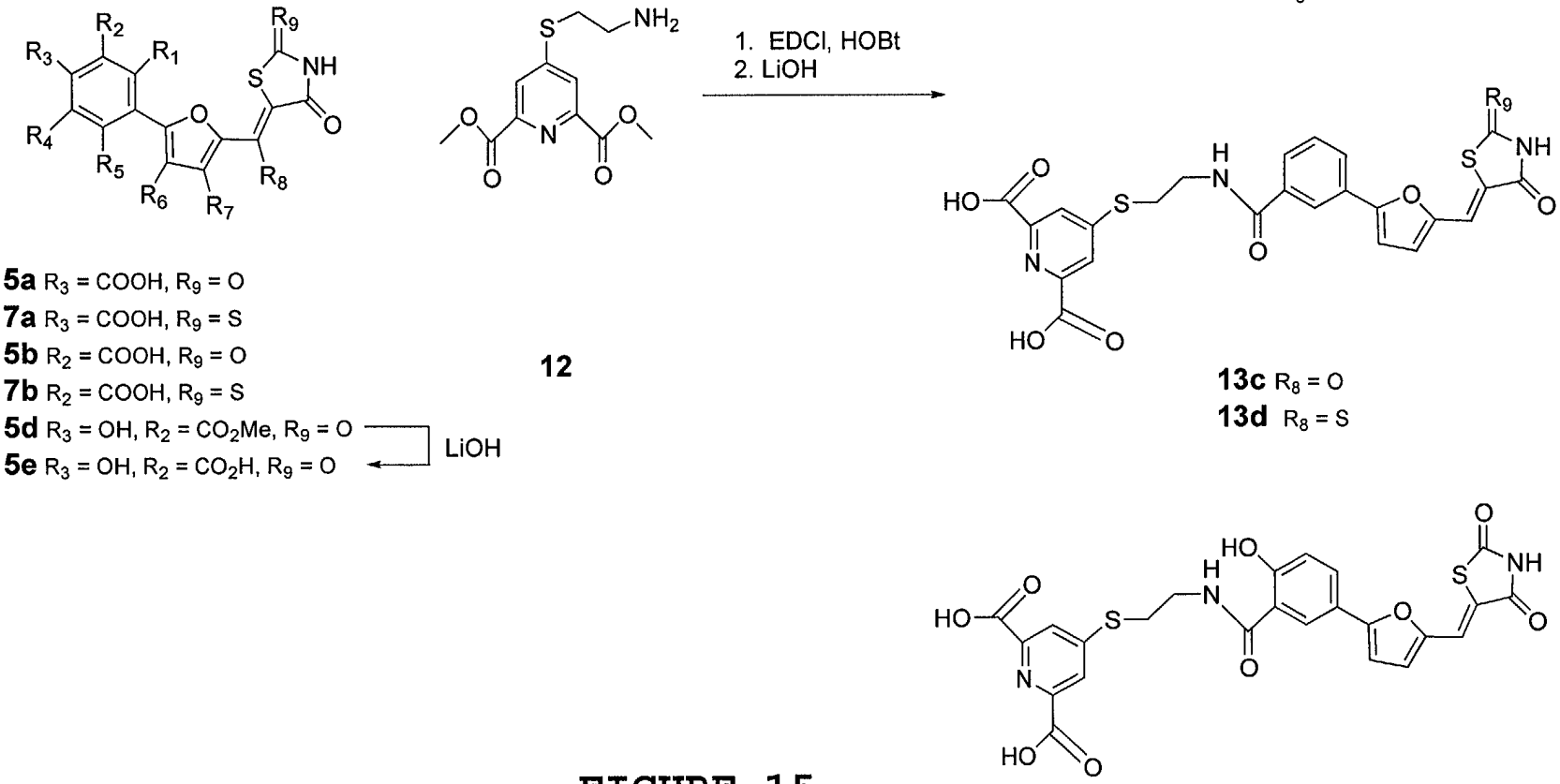


FIGURE 15

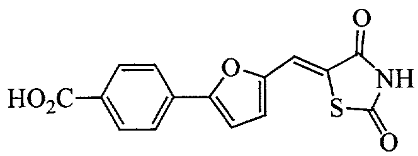
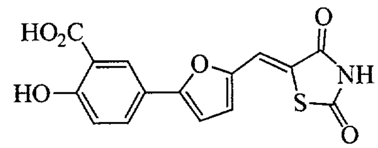
	5a	5e
Structure		
DHPR IC_{50}	> 200 µM	> 200 µM
LDH IC_{50}	Not tested	46 µM
ADH IC_{50}	116 µM	21 µM
DHFR IC_{50}	> 75 µM	Not tested
DOXPR IC_{50}	> 200 µM	> 100 µM
GAPDH IC_{50}	> 200 µM	> 200 µM
IPMDH IC_{50}	Not tested	> 50 µM
IMPDH IC_{50}	> 200 µM	2.15 µM
AR IC_{50}	2.26 µM	No inhibi-tion
HMGCoAR IC_{50}	49.3 µM	245 nM

FIGURE 16

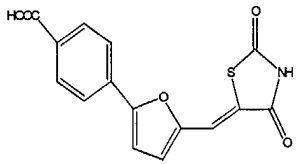
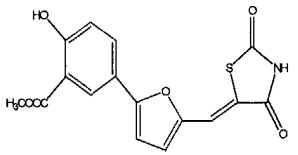
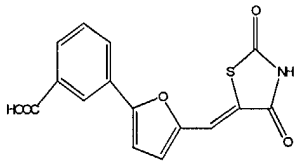
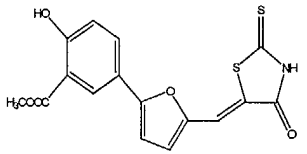
Structure				
HMGCoAR	1.75 μM	245 nM	> 400 μM	143 nM
IMPDH	58.8 μM	2.15 μM	No inhibition	Not tested
DOXPR	52.2 μM	> 100 μM	> 400 μM	1.6 μM
DHPR	> 150 μM	> 200 μM	> 400 μM	2.1 μM
DHFR	No inhibition	No inhibition	> 400 μM	4.3 μM
IPMDH	> 200 μM	> 50 μM	Not tested	Not tested
GAPDH	> 100 μM	> 200 μM	> 400 μM	Not tested
AR	4.1 μM	No inhibition	Not tested	Not tested
ADH	140 μM	21 μM	Not tested	3.4 μM
LDH	Not tested	46 μM	Not tested	340 nM

FIGURE 17

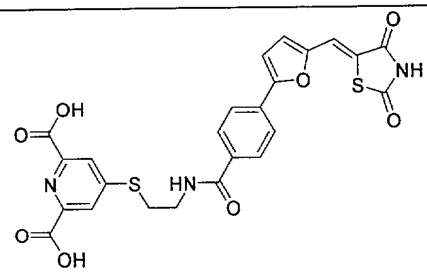
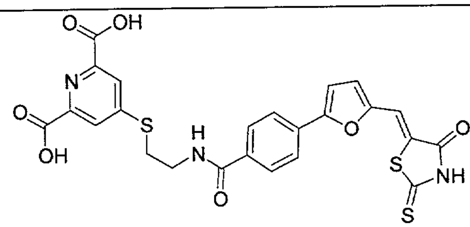
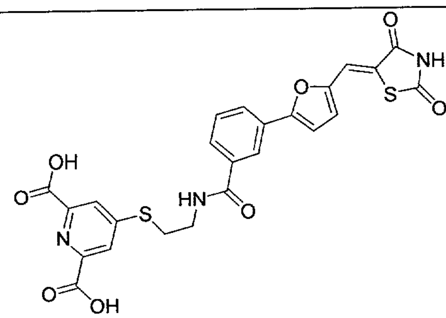
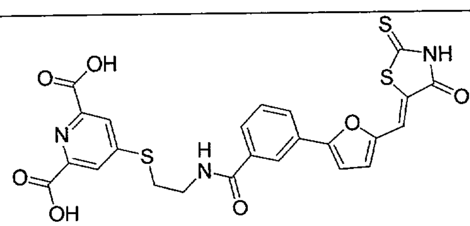
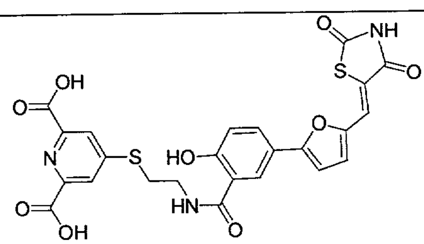
Compound	Chemical structure	IC_{50} for DHPR (μM)
13a		0.536
13b		7.1
13c		13.0
13d		0.254
13f		4.91

FIGURE 18

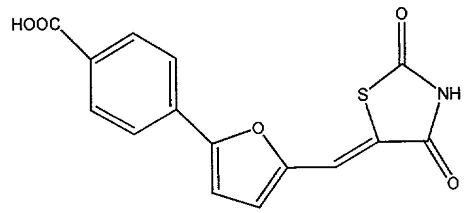
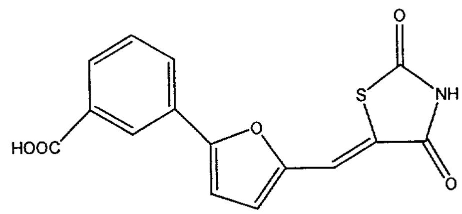
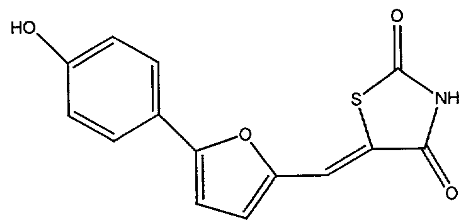
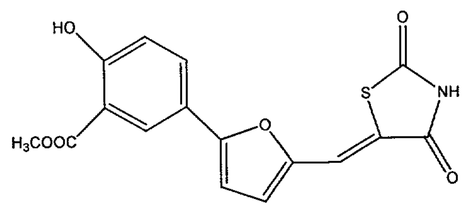
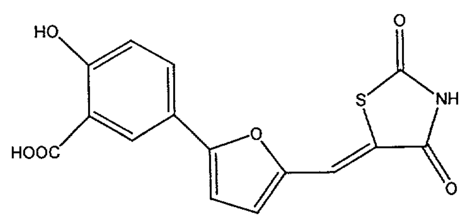
Compound #	Compound Name	Structure
5a	4-[5-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]benzoic acid	
5b	3-[5-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]benzoic acid	
5c	5-[5-(4-hydroxy-phenyl)-furan-2-ylmethylene]-thiazolidine-2,4-dione	
5d	5-[5-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]-2-hydroxy-benzoic acid methyl ester	
5e	5-[5-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]-2-hydroxy-benzoic acid	

FIGURE 19a

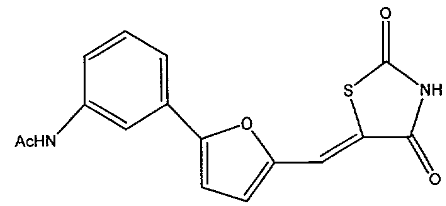
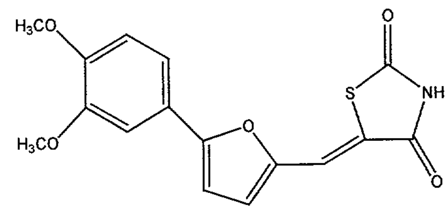
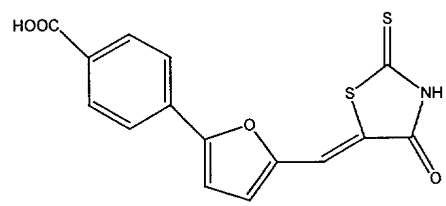
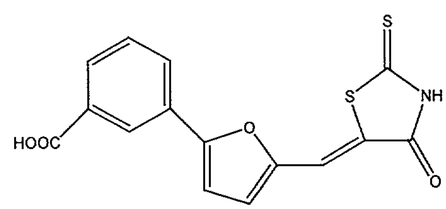
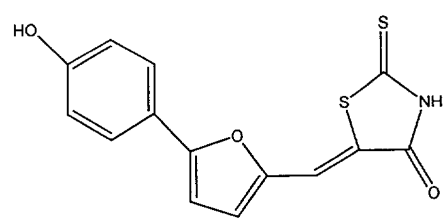
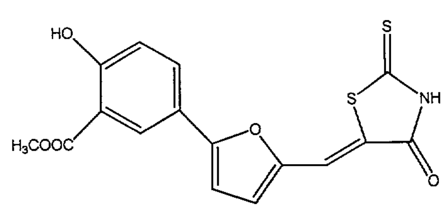
5f	N-{3-[5-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]phenyl}acetamide	
5g	5-[5-(3,4-dimethoxy-phenyl)-furan-2-ylmethylene]-thiazolidine-2,4-dione	
7a	4-[5-(4-oxo-2-thioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]benzoic acid	
7b	3-[5-(4-oxo-2-thioxo-thiazolidin-5-ylidenemethyl)-furan-2-yl]benzoic acid	
7c	5-[5-(4-hydroxy-phenyl)-furan-2-ylmethylene]-2-thioxo-thiazolidin-4-one	
7d	2-hydroxy-5-[5-(4-oxo-2-thioxo-thizolidine-5-ylidenemethyl)-furan-2-yl]-2-benzoic acid methyl ester	

FIGURE 19b

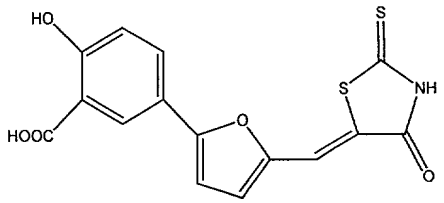
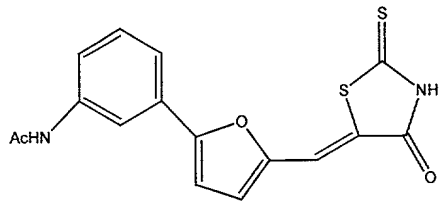
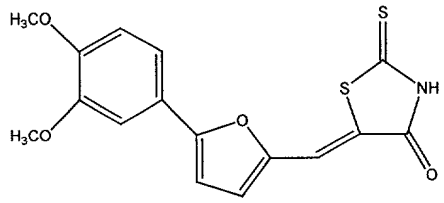
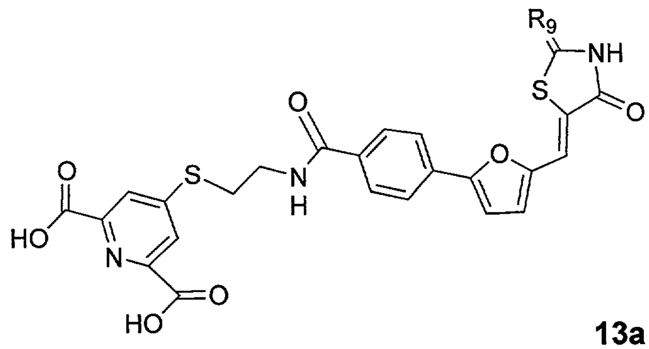
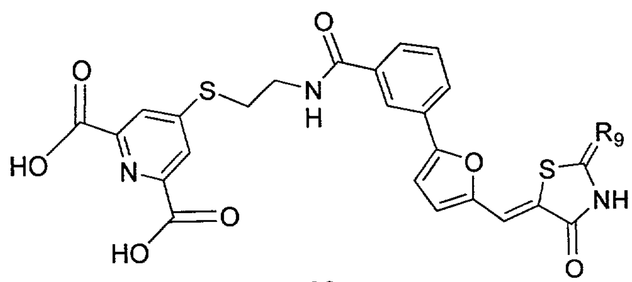
7e	2-hydroxy-5-[5-(4-oxo-2-thioxo-thiazolidine-5-ylidenemethyl)-furan-2-yl]-2-benzoic acid	
7f	N-{3-[5-(4-oxo-2-thioxo)-thiazolidin-5-ylidenemethyl)-furan-2-yl]phenyl}acetamide	
7g	5-[5-(3,4-dimethoxy-phenyl)-furan-2-ylmethylene]-2-thioxo-thiazolidin-4-one	

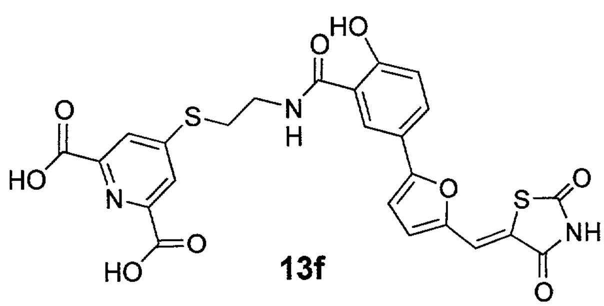
FIGURE 19c



13a R_9 = O
13b R_9 = S



13c R_9 = O
13d R_9 = S



13f

FIGURE 20